Bradshaw, C. S., Horner, P. J., Jensen, J., & White, P. J. (2018). Syndromic management of sexually-transmitted infections and the threat of untreatable Mycoplasma genitalium. *Lancet Infectious Diseases*, *18*(3), 251-252. https://doi.org/10.1016/S1473-3099(18)30080-X

Syndromic management of sexually-transmitted infections and the threat of untreatable *Mycoplasma genitalium*

Lancet Infectious Diseases 2018; 18(3): 251–252. http://dx.doi.org/10.1016/S1473-3099(18)30080-X

Takashi Deguchi[1] describes issues in syndromic management of sexually-transmitted infections (STIs) and in particular treatment of *Mycoplasma genitalium*, which shows increasing drug resistance, especially in Asia-Pacific, and may become the first untreatable STI.[2] Widespread syndromic use of azithromycin has increased macrolide resistance in several bacterial STIs, and the evidence that macrolide resistance is less likely to develop with an "extended" azithromycin regimen as suggested by Deguchi[1] is not strong.[3] We clearly need to replace syndromic approaches with aetiologic management, which will be facilitated by point-of-care tests, which also need to determine drug-resistance profiles for STIs such as *M. genitalium* and *N.gonorrhoeae*.[4]

However, there is an urgent need to establish guidelines for testing, to avoid widespread asymptomatic screening for *M. genitalium.* Although *M. genitalium* has similar prevalence to *C.trachomatis,*[2] screening cannot currently be recommended, due to uncertainty in *M. genitalium*'s natural history causing large uncertainty in the potential benefits,[5,6] and concern about selection for antimicrobial resistance, and drug toxicity.[7] Treatment of *M. genitalium* is becoming increasingly challenging with resistant cases requiring costly drugs, which often have limited availability and are associated with rare but serious side effects.[1,2]

Until more-effective and tolerable regimens exist we recommend that sexual health services should avoid unnecessarily identifying asymptomatic infections, due to the consequent imperative to treat. The only patients where testing for *M. genitalium* is clearly indicated are (i) those with symptoms (urethritis, cervicitis, pelvic inflammatory disease[7]), and (ii) *current* partners of index patients infected with *M. genitalium* (even if asymptomatic), to prevent potential reinfection. Multiplex tests detecting *M. genitalium*[8] should not be routinely used for sexual health patients without disease since this would create a *de facto* screening programme. However, more information is needed to better-understand *M. genitalium*'s natural history, and unlinked anonymous monitoring of samples from asymptomatic patients tested for other STIs would provide valuable information, including rates of *M. genitalium* co-infection with *C. trachomatis* and *N. gonorrhoeae* to inform treatment guidelines.[6] Treatment of *C. trachomatis* and *N. gonorrhoeae* with azithromycin will select for resistance in patients co-infected with *M. genitalium* and this use needs to be reviewed.

To manage *M. genitalium* effectively, testing should always include the antimicrobial resistance profile: antimicrobial resistance is the primary cause of treatment failure with azithromycin and quinolones.[3] Treatment should always be followed by test-of-cure: treatment failures may have a reduced bacterial load and mild/unnoticed symptoms, creating an opportunity for propagation of resistance.

1. Deguchi T. Proposed treatment strategies for non-gonococcal urethritis. *Lancet Infect Dis* 2017; 17: 1121-1122. https://doi.org/10.1016/S1473-3099(17)30571-6

2. Jensen JS. *Mycoplasma genitalium*: yet another challenging STI. *Lancet Infect Dis* 2017; 17: 795–96. https://doi.org/10.1016/S1473-3099(17)30364-X

3. Horner P, Ingle SM, Garrett F, Blee K, Kong F, Muir P, et al. Which azithromycin regimen should be used for treating *Mycoplasma genitalium*? A meta-analysis. *Sex Transm Infect* 2017; Epub ahead of print https://doi.org/10.1136/sextrans-2016-053060

4. Sadiq ST, Mazzaferri F, Unemo M. Rapid accurate point-of-care tests combining diagnostics and antimicrobial resistance prediction for *Neisseria gonorrhoeae* and *Mycoplasma genitalium*. *Sex Transm Infect* 2017; 93(S4):S65-S68. https://doi.org/10.1136/sextrans-2016-053072

5. Smieszek T, White PJ. Apparently-different Clearance Rates from Cohort Studies of *Mycoplasma genitalium* are Consistent after Accounting for Incidence of Infection, Recurrent Infection, and Study Design. *PLoS ONE* 2016; 11(2): e0149087. https://doi.org/10.1371/journal.pone.0149087.

6. Birger R, Saunders J, Estcourt C, Sutton AJ, Mercer CH, Roberts T, White PJ. Should we screen for the sexually-transmitted infection *Mycoplasma genitalium*? Evidence synthesis using a transmission-dynamic model. *Sci Rep* 2017; 7: 16162. https://doi.org/10.1038/s41598-017-16302-8

7. Golden MR, Workowski KA, Bolan G. Developing a Public Health Response to *Mycoplasma genitalium*. *J Infect Dis* 2017; 216 (Suppl 2): S420-S426. https://doi.org/10.1093/infdis/jix200

8. Gaydos CA. *Mycoplasma genitalium*: Accurate Diagnosis Is Necessary for Adequate Treatment. *J Infect Dis* 2017; 216 (Suppl 2): S406-S411. https://doi.org/10.1093/infdis/jix104

Catriona S Bradshaw[1,2], Patrick J Horner[3,4,5], Jørgen S Jensen[6] , Peter J White[7,8*]

*Corresponding author: p.white@imperial.ac.uk

[1]Central Clinical School, Monash University, Melbourne, Australia

[2]Melbourne Sexual Health Centre, Alfred Hospital, Melbourne, Australia

[3]Population Health Sciences, University of Bristol, Bristol, UK

[4]Unity Sexual Health, University Hospitals Bristol NHS Trust, Bristol, UK

[5]National Institute for Health Research Health Protection Research Unit in Evaluation of Interventions, University of Bristol, Bristol, UK

[6]Research Unit for Reproductive Microbiology, Statens Serum Institut, DK-2300 Copenhagen S, Denmark

[7]MRC Centre for Outbreak Analysis and Modelling and NIHR Health Protection Research Unit in Modelling Methodology, Imperial College London, London, UK

[8]Modelling and Economics Unit, National Infection Service, Public Health England, London, UK

CSB declares no personal competing interests and declares institutional funding for a research nurse from SpeeDx Pty Ltd. PJH declares no personal competing interests and declares institutional funding to the University of Bristol for travel, educational activities and advice from Hologic. JSJ has received speaker's fee from Hologic and serves a scientific advisory board of Roche Mulecular Systems. SSI has received remuneration for contract work from SpeeDx, Hologic, NYTor, Diagenode, Nabriva, GSK, and Angelini. PJW declares no competing interests.

PJH thanks the UK National Institute for Health Research (NIHR) Health Protection Research Unit (HPRU) in Evaluation of Interventions (HPRU-2012-10026) at the University of Bristol, and PJW thanks the NIHR HPRU in Modelling Methodology (HPRU-2012-10080) at Imperial College London, both in partnership with Public Health England, for funding. PJW also thanks the Medical Research Council (MR/K010174/1) for funding.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The views expressed are those of the authors and not necessarily those of the Department of Health, Medical Research Council, NHS, NIHR, or Public Health England.